Digitized by the Internet Archive
in 2010 with funding from
University of Toronto

http://www.archive.org/details/n7transactionsof09roya

STORAGE

VOL. IX. No. 7 JUNE, 1916

TRANSACTIONS

OF THE

ROYAL

SOCIETY OF TROPICAL MEDICINE AND HYGIENE.

London:
SOCIETY OF TROPICAL MEDICINE AND HYGIENE,
11, CHANDOS STREET, CAVENDISH SQUARE, W.

TRANSACTIONS

OF THE

SOCIETY OF TROPICAL MEDICINE AND HYGIENE.

JUNE, 1916.

VOLUME IX. No. 7.

Proceedings of a Meeting of the Society held on Friday, May 19th, 1916, at 5.30 p.m., at 11, Chandos Street, Cavendish Square, W., Surgeon-General Sir DAVID BRUCE, C.B., A.M.S. (*Vice-President*), in the Chair.

CEREBRO-SPINAL FEVER, WITH NOTES OF SOME CASES.

BY

MAJOR J. M. ATKINSON, R.A.M.C.

(Officer in Charge, Richmond Military Hospital).

It occurred to me that a discussion on this disease, which has only become really prevalent in England since the commencement of the War, would prove of interest to the members of this Society.

It is only since the winter of 1914-15 that cerebro-spinal fever has become epidemic in this country.

Prior to this date it was sporadic. This fact is clearly shewn by the Reports of Surgeon-Colonel REECE, one of the Medical Officers of the Local Government Board, who was deputed to collate and report to the Board annually on its prevalence. There were notified in the civil population in England and Wales, during the year 1913, 279 cases of cerebro-spinal fever; in 1914 there came to notice 300 cases. The greatest incidence fell in children under fifteen years of age (80·6 per cent.). The case fatality was high, the mortality rate being 69·6 per cent. in the former years, and, in 1914, 68·7 per cent.

Cerebro-spinal fever is much more prevalent in the United States of America and Canada than in this country, and undoubtedly one of the most important factors that contributed to its prevalence in an epidemic form in the British Isles was the concentration of troops at various centres in this country, and more especially the arrival of the Canadian troops—this was undoubtedly an important factor in the subsequent prevalence of the disease.

To most members of our profession, prior to 1914-15, this disease was only known by name.

DEFINITION.

Cerebro-spinal fever may be defined as a specific disease due to infection of the organism by the *Diplococcus meningitidis* of WEICHSELBAUM, occurring both in epidemic and in sporadic form, and most often shewing itself as a meningitis involving the whole cerebro-spinal axis.

HISTORY.

The first authentic account of an epidemic is that which occurred in Geneva in 1805. Glimpses of the disease, in this epidemic form, are met with in the literature of the Middle Ages.

The epidemic in Geneva does not appear to have been widespread, as only thirty-three persons died of the disease.

The interest lies in the contemporary records: the clinical symptoms were accurately described by VIEUSSEUX, as well as the post-mortem appearances by MATTHEY.

VIEUSSEUX writes: "The initial symptom was a sudden failure of strength; the expression was anxious; the pulse was feeble, sometimes threadlike, in a few cases hard and bounding. There was violent headache—in the main, frontal.

"The headache was followed by the vomiting of green matter, by stiffness of the spine, and, in infants, by convulsions.

"The body shewed livid patches after death—occasionally, during life."

MATTHEY well describes the post-mortem appearances: "The vessels of the meninges," he says, "were notably congested; a gelatinous humour covering the brain was markedly tinged with blood. There was fluid in the ventricles. The choroid plexus was of a deep-red colour.

"The base of the brain was covered by yellow puriform matter, with no obvious change in the underlying cerebral tissue. The exudation covered the optic chiasma and extended backwards towards the cerebellum, reaching for the space of an inch down the vertebral canal."

The subsequent history of the disease is well described in FOSTER and GASKELL'S monograph published this year.

Read in the light of our present knowledge, the part played by the carrier in the spread of the disease affords a clear explanation of the records of these long past epidemics.

Assuming the presence of a few permanent carriers, it only requires outside conditions which facilitate the spread of the organisms to create a large number of temporary carriers, in other words, "the number of the carriers constitutes the epidemic."

The persons who fall sick of the disease are thus but the concrete evidence of the wide diffusion of temporary carriers.

The disease spread to Canada in 1807, to Virginia, Kentucky and Ohio in 1808, appearing in "the State of New York" and in Pennsylvania in 1809.

This American epidemic was remarkable in the giving of it the name of "spotted fever," by which name it is described in a book entitled, *Treatise on a Malignant Epidemic called Spotted Fever*, written by NORTH in 1811.

During this period the disease was rife in Europe also.

In 1806-7 it broke out in the Prussian Army, amongst the Spanish prisoners at Brianca, at Brest in 1813, and at Paris in 1814. These epidemics coincided with several outbreaks of typhus fever, with which the cases of cerebro-spinal fever were often confounded.

Between 1837-1850 a very wide-spread epidemic appeared in France, the disease being carried from place to place by the transfer of troops.

The years 1851-61 included a large epidemic in Norway and Sweden; in the years during which the disease raged it caused no less than 4,138 deaths in Sweden, where only two provinces out of twenty-four, and those the most northerly, escaped.

Coming down to recent years (1905-15), there has been a revival of the disease in an epidemic form over a very large area. This revival of cases appeared to have started by the large outbreak which occurred in the United States in 1904.

New York, in the year 1905, had no fewer than 2,755 cases. Two years later, an almost equally severe outbreak occurred at Glasgow, at Edinburgh, and at Belfast.

The New York epidemic gave FLEXNER full scope for trial of the serum manufactured according to his method and tested on monkeys.

This period in the history of the disease produced important bacteriological researches, establishing beyond reasonable doubt the causative nature of WEICHSELBAUM'S coccus, and completing our knowledge of its cultural and bio-chemical, characters.

The same period also saw the evolution of the doctrine of the carrier, a doctrine which affords the most satisfactory solution of the problem of the dissemination of the disease.

The most recent experiences of the disease are that of the present epidemics in England and in France. At various barracks and camps the disease has appeared, and, as usual, the armies in the field have almost entirely escaped.

Civilians have also suffered, a good deal of evidence going to shew that some of the soldiers have acted as carriers whilst in billets, and when on leave.

The coincidence of severe outbreaks of influenza have contributed an additional catarrhal factor in connection with the epidemiology of the present outbreak of cerebro-spinal fever.

It is principally a disease of towns. Surgeon-Colonel REECE in his notes on the prevalence of cerebro-spinal fever during the last four months of 1914, and the first six months of 1915 *(Journal of the Royal Army Medical Corps for June, 1915)*, gives the percentages as follows:—

Urban Districts	66·3.
Rural Districts	10·3.
London	23·3.

It is protean in nature. The period of incidence decreases with advancing age.

From the same paper I find that the first military case in 1914 was that of a Somerset Yeoman at Great Bentley, in Essex. The first symptoms of illness occurred on 19th September, 1914, he went home to Taunton on 23rd September, and died there on October 14th.

The next, of 18th October, 1914, was a soldier of the Canadian contingent in the Bustard Camp on Salisbury Plain. There had been

four cases of cerebro-spinal fever amongst the Canadian troops while in Canada and before embarkation; three cases occurred during the voyage, two, a soldier and a steward's clerk on a transport, and one soldier on another.

This case came from a transport on board of which no case occurred during the voyage. Three more cases occurred amongst the Canadians on the Plain on the following dates respectively—27th October, 30th October, and the 4th November, 1914.

Between January 9th, 1915, and July 31st, 1915, there was quite an epidemic, the following being the number of cases that were notified:—Civilians, 2,290; Troops, 1,088; the highest incidence being in the week ending March 13th, 1915, the numbers notified for that week being:—Civilians, 147; Troops, 87.

SYMPTOMS.

Incubation.—The period of incubation varies from three to five days. The former limit would appear to be the more usual period, while in the malignant forms this may be still further shortened. The number of cases on which it may be gauged are few.

Invasion.—The onset is, as a rule, sudden, frequently being ushered in by a rigor, then follow the usual symptoms of an acute specific fever, viz., a temperature of 102° F. to 104° F., usually rising rapidly, and attaining to a fairly high degree on the first day.

A short period of general malaise is succeeded by headache, which is often intense. A striking feature in many cases is complete loss of appetite, amounting even to absolute revulsion against any kind of food; this is frequently followed by vomiting, then follow pains in the neck and limbs, retraction of the head, and some degree of catarrh of the nose, throat, eye or ear.

In severe cases delirium soon supervenes, followed by coma and death. There is a peculiar distinctive cry about this delirium.

The height of the temperature forms no criterion of the severity of the disease, some of the most rapidly fatal cases shewing but a very slight rise. The pulse is usually quickened, but as a rule not to the extent which would be expected from the temperature. The occurrence of a pulse of 60 to 80 accompanying a temperature of 101° F. to 103° F.

is not uncommon in the early stages of the disease, and is of considerable diagnostic importance.

Eruption Stage.—This usually appears during the first week and may be macular, erythematous, petechial or purpuric.

The maculæ do not come out in successive crops, begin to fade rapidly, and disappear usually in four days.

The erythematous rash is like the transient erythema which may precede the eruption in small pox or typhus. Like the maculæ they may appear at any part of the body.

When petechiæ and a purpuric rash appear, they are evidence of profound toxæmia.

Herpes is common. There is usually some leucocytosis—20,000 to 40,000 per c.mm. Kernig's sign is present; this occurs in all but the fulminant cases, it is one of the earliest symptoms to appear. The pupils are usually dilated, they may be unequal. Towards the end of the first week a condition of semi-stupor occurs, accompanied by marked retraction of the head. The temperature remains fairly high and approaches to the continued type.

The patient remains quite the same for two or three weeks and recovery is very gradual; ultimately the fever completely subsides, the headache and stupor pass off and the rigidities shortly disappear; the actual convalescent stage once being established is rarely interrupted, it may be weeks before the patient is free from stiffness. Unfortunately paralysis of single muscles, or of groups of muscles, may remain. Permanent deafness and blindness are by no means uncommon, and in some cases the patient never recovers his mental power and remains an imbecile.

DIAGNOSIS.

WEICHSELBAUM discovered the meningococcus in 1887; QUINCKE introduced lumbar puncture in 1890. It is the presence of the diplococcus of WEICHSELBAUM in the cerebro-spinal fluid that establishes the diagnosis.

The disease with which it is most often mistaken is influenza; fever prolonged past the seventh day, in the absence of any complication is unlikely to be due to influenza.

There is not time to go into the differential diagnosis. However,

I would mention that in typhoid the headache usually ceases when delirium commences, but in this disease it is not so.

BACTERIOLOGY.

It is the presence of WEICHSELBAUM'S gram-negative diplococcus in the cerebro-spinal fluid, obtained by lumbar puncture, that clenches the diagnosis, and fulfils all KOCH'S postulates; it can be grown outside the body in pure culture, it is capable of producing the disease when injected into susceptible animals, and it can be recovered from the lesions so produced and again cultivated outside the body.

During the first fortnight of the disease the meningococcus can usually be recovered from the naso-pharynx.

The organisms are generally almost entirely intra-cellular, lying within the bodies of the polymorphonuclear leucocytes; but there are exceptions; they may be more numerous in the fluid. The number of cocci in the cerebro-spinal fluid varies very much in different cases, and also in individual cases in the stage of the disease; though earlier the disease as a rule, the fewer the meningococci.

The differential characters of the meningococcus are :—

(a) The majority of strains of meningococci fail to grow on ordinary media at a temperature below 25° C.

(b) The meningococcus ferments glucose and maltose with the production of an acid reaction, but fails to change saccharose.

(c) The meningococcus shews positive agglutination with homologous antimeningococcal serum, and has the capacity of removing or absorbing the specific agglutinin from such serum.

The last appears to be the most valuable of available positive tests for identifying the meningococcus. It is necessary, however, to do a control test with normal serum, and also with a suspension of homologous meningococci.

The specific agglutinating serum used for testing suspect meningococci from the naso-pharynx of contacts should be of proved activity, not only against strains of meningococcus from the same outbreak, but also against strains from the cerebro-spinal fluid of recent cases of cerebro-spinal fever in the district where the disease is manifesting itself.

Lieut.-Col. MERVYN GORDON has shewn that in the present epidemic there are four or more distinct strains of virulent meningococci.

TREATMENT.

Antimeningococcal serum should be injected intraspinally after the removal of an equal amount of cerebro-spinal fluid. The serum should be warmed to the body temperature, at least 20 c.c. injected, and the foot of the bed should be raised after the injection. The dose should be repeated daily if necessary. The indication for further serum should be the turbidity of the fluid drawn off; if it is still turbid it is well to give more serum. Intercurrent conditions should be treated as they arise, special care being taken of the eyes. The indication for further serum is proportionate to the number of the meningococci still present, as found by examining a film of the withdrawn cerebro-spinal fluid.

Many aver that mere lumbar puncture without the injection of any serum is, in many cases, curative. Should the disease be met with sufficiently early, treatment by daily lumbar puncture would hold out considerable hope of success. Our failure, in the first months of the present epidemic, to secure the excellent results attained by serum injection in America was apparently due to the fact that we relied largely on sera obtained from American sources; whereas the types of meningococci prevailing in this epidemic differed from those found in the United States.

MORTALITY.

The mortality in cerebro-spinal fever is undoubtedly higher in the epidemic than in the sporadic cases. In epidemics, the mortality prior to the introduction of serum treatment was about 70 to 80 per cent. Since the serum treatment, the mortality in epidemics has fallen to about 30 to 40 per cent.

CARRIERS.

Carriers have been already discussed, but the spread of an epidemic of cerebro-spinal fever is not explained by the discovery of the coccus in the naso-pharynx of *actual* patients, for disease rarely spreads by direct contact from patient to patient.

This difficulty was solved when ALBRECHT and GHON found that the

coccus could be isolated from the naso-pharnyx of healthy persons living in epidemic zones.

In other words, they isolated the meningococcus from healthy contacts; for every case of cerebro-spinal fever there exist in times of epidemic a number of healthy carriers variously estimated at from ten to thirty.

The number of contacts varies with several inconstant factors:—

1. There is a seasonal incidence for carriers as there is for cases; there are twice as many carriers in the spring months as in the summer months.

2. The number of carriers varies also with the stage, and with the character of the epidemic; there are more carriers when the epidemic is fully developed than during the waxing and waning stages, and there are also more carriers when the epidemic is severe than when it is mild.

3. The closeness of contact between the individuals affects the number of carriers: mothers who nurse their meningotic infants are found to be carriers almost invariably, and carriers are particularly abundant in schools and barracks.

The conditions under which the meningococcus is carried in the throat are very similar to those of diphtheria carriers where also the organisms' stay in the throat may be temporary or prolonged.

In diphtheria the organism may exist in some for years.

The limit with the meningococcus as far as it is at present known is six months. Surgeon-Colonel REECE tells me of one case in which it has lasted for a year, and another case, like "Charley's Aunt," is still running.

A temporary carrier is comparatively easy to deal with. The organism seldom survives for as long as a fortnight in the throat; contacts giving two negative results may be discharged to duty.

In a number of cases the first swab is positive, while the second swab, taken some ten days later, and all subsequent swabs, proved negative. The period of isolation required in such a case is, therefore, short.

Prolonged carriers are very much more difficult to deal with, as it is hardly practicable even in the case of troops to isolate an individual for

as long as six months; this problem is still without a satisfactory solution.

TECHNIQUE OF PASSING THE NASO-PHARYNGEAL SWABS.

Two matters are of prime importance in this connection:—

1. The swab should be as free as possible of contamination with saliva.

2. As the meningococcus readily dies on the swab, it is desirable to make the cultures as quickly as possible, and for these cultures to be got into the incubator as quickly as possible.

With a view to avoidance of contamination by saliva, a special covered swab such as that introduced by WEST is suitable. The man is seated facing the light. His mouth is opened as wide as possible, and the tongue depressed with a spatula. During phonation the covering tube containing the swab is passed behind the soft palate, and the swab extruded so as to come in contact with the naso-pharynx. The swab is then drawn back into the covering tube and the instrument removed.

PUBLIC HEALTH PRECAUTIONS.

Prevention.—The meningococcus is spread by being carried in the nose and throat of normal individuals, convalescent patients, and patients actually suffering from the disease, and is imparted to other individuals by direct contagion.

Such contagion takes place either by actual contact, such as kissing, or by spraying of the discharges of the throat and nose, as in coughing, speaking, singing and sneezing. The question of preventive measures, therefore, resolves itself into the isolation and treatment of such persons. The average period of time during which a person may carry the active infection in his naso-pharynx is twenty-one days; a fairly trustworthy result should be available in four or five days; this is a very important result as regards military efficiency, as it means a saving of seventeen days for each contact who has been found positive.

There is also a possibility that the organism might be spread by the contamination of articles of clothing, or of walls and floors by such proceedings as spitting, but the extreme susceptibility of the meningococcus to drying renders such method of spread at least very unlikely. The

utensils used in food, such as cups, spoons, etc., may undoubtedly spread the infection.

The fact that by far the greater number of carriers have normal throats, therefore no excessive discharge from the nose or posterior naso-pharynx, and thus little inclination to indulge in spitting, is an additional factor in making such a method of spread improbable.

The treatment of convalescent cases, as regards the possibility of their spreading infection, is similar to that of carriers.

There is no reason why positive contacts should not be allowed to take exercise in the open air, provided they are isolated from their fellow-creatures, and care is taken to mark their food utensils.

Prophylaxis.—Prophylaxis for the healthy individual resolves itself into the use of general hygienic measures, especially avoiding cold, catarrhal affections and overcrowding.

In epidemic areas, schools should close, and troops leave barracks for roomy huts or tents in the open air: provided in each case there is no incidence of the disease nor occurrence of carriers amongst the individuals concerned. The billeting of soldiers upon civilians should cease.

Notes of Bacteriologist *re* the Richmond Military Hospital Cases.

(For these Notes, I am indebted to Captain M. W. Flack, R.A.M.C., Bacteriologist at Millbank.)

In the diagnosis of the following four cases, and in the bacteriological examination of their contacts, the Millbank medium, consisting of trypsinised ox heart broth, to which agar and an extract of pea-flour are subsequently added, has been used throughout—before pouring, 2 per cent. of ordinary horse serum is added. When endeavouring to grow the meningococcus from the cerebro-spinal fluid of the patient, a little fresh human blood is spread over the surface of the medium.

The examination of contacts is performed by swabbing their naso-pharynx (using a West's swab) and plating the swab *immediately*. The plates are incubated for 24 hours, and suspicious colonies of gram-negative cocci are subcultured on plates. These are incubated for another 24 hours.

The resulting growth is washed off and emulsions prepared with saline, and, in order to inactivate the antolysin, are heated for half an hour at a temperature of 65° C. They are then standardised to a strength of 2,000 million per c.c. and 5 per cent. of phenol added; with the predominate types of meningococci of last year's epidemic, high titre agglutinating sera have been prepared. The emulsions are tested against these, and, if necessary, the result can be confirmed by the absorption of agglutinin.

Case 1.—Pte. X., Y Regt., came in from parade on Friday, December 13th, 1915, complaining that he felt queer and went to bed early. During the night he became delirious, was very violent, and vomited occasionally. He was transferred from his billet to Richmond Military Hospital at about 1 a.m., December 18th. Just before death, lumbar puncture was performed, and a turbid purulent fluid was drawn off.

Microscopically the fluid shewed masses of polymorphonuclear leucocytes and numerous gram-negative cocci, both extra-cellular and a few intra-cellular. Culturally the fluid yielded an abundant growth of gram-negative cocci. An emulsion was prepared and the coccus submitted to the agglutination test. The organism proved to be a Type I. meningococcus, which result was subsequently confirmed by absorption.

Four contacts from the billet, three intimate friends of deceased and two R.A.M.C. orderlies from Richmond Military Hospital were swabbed. These were all found to be negative. From four swabs suspicious gram-negative cocci were obtained, which the agglutination shewed to be negative.

Case 2.—Driv. X., Y Regt., was sent to the Richmond Military Hospital on February 19th, 1916, suffering from what was suspected to be acute rheumatism. He complained of severe pains in head and bottom of back, accompanied by vomiting. On February 22nd, cerebro-spinal fever was suspected and he was isolated. Lumbar puncture was performed and turbid cerebro-spinal fluid was removed. Microscopically the fluid shewed many polymorphonuclear leucocytes and both extra- and intra-cellular gram-negative cocci. On blood plates a growth of meningococcus was obtained, which was shewn by agglutination to be of Type II. See Table I. A coccus of the same type was isolated from his naso-pharynx.

After diagnosis the man was removed to Fulham Military Hospital,

where he was given several doses of the new military anti-meningococcal serum, prepared at the Lister Institute from the types of meningococci, prevalent in last year's epidemic. The patient reacted well to the serum, and he recovered rapidly and completely. Also his naso-pharynx cleared up speedily, and he was declared negative on April 6th, 1916, and was discharged from Fulham Military Hospital to a Convalescent Hospital.

At Burvale House, Hersham, where the patient was stationed, eighteen contacts were examined, mainly those who occupied the same bedroom. The R.A.M.C. orderly, who attended this man from the time he was taken ill until he was transferred to Richmond, was included. Of these eighteen, twelve were declared negative on first examination of the plates, and six suspicious cocci were subcultured for agglutination. As the attached Table I. shews, they were positive and of the same type meningococcus as the case.

At Richmond Military Hospital, of twelve contacts examined, three shewed suspicious gram-negative cocci, which were subsequently raised for agglutination. One proved to be positive and of the same type as that of the case.

Of the three positive contacts at Burvale House, one slept in the next bed, one exactly opposite, and the third—the R.A.M.C. orderly who attended him—in the same room.

The positive contact at Richmond Military Hospital was in the same ward and in attendance on the patient. The four positive contacts were transferred to carrier wards. The R.A.M.C. orderly cleared up almost immediately; one Burvale House carrier was discharged after two negative swabs on April 18th; the other Burvale House carrier is still in quarantine (end of April); and the Richmond contact was discharged on April 21st after two negative swabs.

Case 3.—2nd A.M. X., Y Regt., stationed at Roehampton, came from Larkhill Camp, Salisbury, on Saturday, 11th March, and, at 7 p.m. on the same day, was suddenly taken ill with excruciating pains in head and back, and vomited on Sunday morning, when he was admitted to Richmond Military Hospital. His temperature on admission was 102 F.* He quickly became delirious and very violent, coma supervening. He died at 2 p.m., soon after lumbar puncture. The fluid drawn off was

* At Larkhill Camp there was a batch of men who had recently arrived from The Curragh, where cerebro-spinal fever was prevalent.

turbid, and shewed microscopically many gram-negative cocci extra- and intra-cellularly. An abundant growth was obtained, and the organism was proved by agglutination to be a Type IV. meningococcus. In all, twenty-nine contacts were examined. These consisted of nineteen men who had slept in the same hut at Roehampton for one night only; the N.C.O. in charge of the hut; five men who had travelled in the same railway carriages as the patient, either from Larkhill to Waterloo or from Waterloo to Barnes; one man who had slept in same hut at Larkhill; and three orderlies from Richmond Military Hospital. Three shewed suspicious cocci, which were submitted to the agglutination test. Two were positive, but only one of the same type as the case, and it is interesting to note that the one true contact was the man who slept in the same hut at Larkhill Camp. The other positive contact must be looked upon as an accidentally found carrier. See Table II. for results.

Case 4.—Pte. Y., E Regt., was admitted into Richmond Military Hospital on March 30th, 1916, and was transferred to Fulham Military Hospital on the same day. He had spent the previous seven days in detention, and before that was on leave, and had slept for one night only in hut 44 at Wimbledon. He complained of intense headache and stiffness of the neck, and of pains practically all over the body more like those of acute rheumatism. His temperature was 102° F., and he also vomited at times. Lumbar puncture was performed and a clear fluid drawn off, which shewed, on examining the centrifugalised deposit, no cocci and few cells; and, in spite of many subsequent endeavours, it has been found impossible to grow it—no organism could be grown. From his naso-pharynx, however, a suspicious organism was isolated, and proved, after agglutination, to be a meningococcus of Type II. The man was, therefore, regarded as a case; this is confirmed by the marked response to serum treatment. Twenty-three contacts were examined; of these, three shewed suspicious gram-negative cocci, which were raised for agglutination. One proved to be positive and of the same type as the case.

Clinical Notes.

Case 1.—Admitted Richmond Military Hospital, 18th December, 1915, complaining of severe headache; vomiting. Temperature on admission, 102·6; pulse only 68.

Kernig's sign present. Lumbar puncture the same day and 20 c.c. of anti-meningococcal serum injected intraspinally.

Fluid turbid. Very somnolent. Became comatose that evening, and died December 19th, 1915.

Case 2.—Admitted 23rd February, 1916, from Richmond. Headache, slight head rigidity, slight Brudzinski, slight Kernig, rational.

Temperature 100°, pupils dilated, vomiting, lumbar puncture at Richmond on 22nd February, 1916.

Lumbar puncture repeated on 24th, 25th and 26th, followed on each of these occasions by administration intrathecally of 30 c.c. of anti-meningococcal serum (Lister).

From the 26th there was steady improvement, and he was discharged to convalescent home on 10th April, 1916.

Case 3.—Admitted to Richmond Military Hospital, 12th March, 1916—on admission, temperature was 102·6 F.—complaining of intense headache with pains in all his limbs. Kernig's sign present. Only came up from Salisbury yesterday; began to feel unwell the same evening.

Was placed in the isolation ward; in a short time became quite maniacal, so much so that it was difficult to restrain him. He had the peculiar cry which I have mentioned before as ushering in the delirium.

The delirium merged into coma, and he succumbed at 2.10 p.m. the same day.

He was lumbar punctured at 1.15 p.m., and 30 c.c. anti-meningococcal serum was injected intraspinally.

Case 4.—Admitted from Wimbledon on 30th March, 1916. Pains all over, severe headache, head rigidity, Kernig's sign, photophobia. Temperature 100°.

Lumbar puncture with administration of Lister serum on 30th and 31st March and April 1st.

On April 1st. Vomiting, semi-conscious, incontinent.

On April 3rd. Great improvement, disappearance of all meningitic signs.

May 3rd. Perfectly well, except that postnasal swab still positive; meningococci present.

TABLE I.—SERA.

Cocci.	N.S.	I. Serum.			N.S.	II. Serum.			
	1/100	1/100	1/200	1/400	1/100	1/100	1/200	1/400	
Standard Sera *v.* Homologous Cocci	–	+ +	+ +	+ +		+ +	+ +	+ +	Controls.
Moore C.S. Fluid ...	–	–	–	–		+ +	+ +	+ +	Positive (II).
Burvale 5	–	–	–	–		(+)	–	–	Negative.
,, 6	–	–	–	–		–	–	–	Negative.
,, 8	–	–	–	–		–	–		Negative.
,, 9	–	–	–	–		+ +	+ +	+	Positive (II).
,, 10	–	–	–	–		+ +	+ +	+ +	Positive (II).
,, 12	–	–	–	–		+ +	+ +	+	Positive (II).
Richmond 8... ...	–	–	–	–		–	–	–	Negative.
,, 9... ...	–	–	–	–		+ +	+ +	+	Positive (II).
Nurse R	–	(+)	–	–		–	–	–	Negative.
Moore N.P.... ...	–	–	–	–		+ +	+ +	+ +	Positive (II).

TABLE II.—SERA.

Cocci.	N.S.	I. Serum.			N.S.	II. Serum.			N.S.	III. Serum.			
	1/100	1/100	1/200	1/400	1/100	1/100	1/200	1/400	1/100	1/100	1/200	1/400	
Standard Sera *v.* Homologous Cocci		+ +	+ +	+ +	–	+ +	+ +	+ +	–	+ +	+ +	+ +	Controls.
Myers C.S. Fluid ...	–	–	–	–		(+)	–	–		+ +	+ +	+	Positive (IV).
Bloomfield	–	–		–		+ +	+ +	+ +		–	–	–	Positive (II).
Carver	–	–	–	–		–	–	–		+ +	+ +	(+)	Positive (IV).
Strive	+	+ +	+ +	+ +		+ +	+ +	+ +		+ +	+ +	+ +	*M. Flavus.*

Note.—N.S. = Normal Serum. N.P. = Naso-Pharynx. It has been shewn that cocci, which agglutinate with normal serum, are *M. Flavus.*

TABLE III.—SERA.

Cocci.	N.S.	I. Serum.			N.S.	II. Serum.			N.S.	III. Serum.			
	$\frac{1}{100}$	$\frac{1}{100}$	$\frac{1}{200}$	$\frac{1}{400}$	$\frac{1}{100}$	$\frac{1}{100}$	$\frac{1}{200}$	$\frac{1}{400}$	$\frac{1}{100}$	$\frac{1}{100}$	$\frac{1}{200}$	$\frac{1}{400}$	
Standard Sera *v.* Homologous Cocci	-	+ +	+ +	+ +		+	+ +	+ +	-	+ +	+ +	+ +	Controls.
Nay N.P.	–	–	–	–		+	–	+		–		–	Positive (II).
P.B. 6...	-	–	-				–						Negative.
,, 7.	-	–	-	–			-	–			-		Negative.
,, 12...	–	-		–		+	+	+					Positive (II).

Note.—N.S = Normal Serum. N.P. = Naso-pharynx. It has been shewn that cocci, which agglutinate with normal serum, are *M. Flavus*.

Fleet-Surgeon P. W. BASSETT-SMITH: As no one else rises, I should like to open the discussion. In the first place I think the question of the bacteriology of cerebro-spinal fever is not quite so plain as is often considered. We know from fact and experience that there are cases where no organism is found in the cerebro-spinal fluid; thus you have cases clinically indistinguishable from cerebro-spinal fever, in which bacteriologically you cannot prove the disease. I only point that out for what it is worth. Of course, that point has been taken strongly hold of by HORT and others. I think at present one ought to have an open mind from the bacteriological point of view on this question. No doubt it seems so plain: you have got your organism which is infective; you have that organism in the cerebro-spinal fluid, blood, throat, etc.; the organisms may be injected into animals, and can be recovered. These are important points; but there is another one: you can get the organism from the throat of the patient suffering with the disease and yet it is apparently not infective. Why is it not infective? At the same time you get from the throat of another person who is quite well, a similar organism, and it is infective. There are many points to be considered besides the organism itself.

Then with regard to carriers. These carriers, when they are prevalent in the different stages of the epidemic, and in different periods of the year, are not, I think, quite so constant as stated. Carriers vary enormously with the character of the people and the health of the individuals. Take for instance a lot of patients at the London hospitals. If you take a number of contacts from these you get a comparatively high number of carriers. You take a number of very healthy men, for instance in a depot for which I have been lately working, where the number of contacts is very low. It depends a great deal on the health and stamina of the people, and more especially on the age of the people. That plays a very important part. For instance, in the London Hospital there are 10 to 20 per cent. of carriers; that calculation was carried out by a high-class bacteriologist. Speaking with a large experience, out of 4,000 cases, my percentage is only 1·3. Every man before being drafted away had to be examined to see whether it was safe or not, and the percentage worked out at 1·4, so that the health of the person, the conditions under which he lives, and his age, are most important points with regard to carriers.

Then another point. Major ATKINSON said he would let a man go after four days with two negative swabs. In the first place I think it is a difficult thing to get the result of the first swab out on the fourth day, and it would take the same period, or longer, to get out the second, so it would not be until about ten days. In the bacteriological description it is stated that the culture is made from the throat direct on to the plate, and grown 24 hours and sub-cultured, and the agglutination tests applied. There is no mention of any fermentation reactions whatever. I should not like to take any positive opinion of any case upon that.

Then another point. Major ATKINSON referred to FLEXNER serum. In a letter I received he (FLEXNER) said the serum was not good, but he thought that was because on the market there was some American serum which was old and was not reliable, and as there has not been an epidemic in America for some time, the serum was consequently not so powerfully anti-toxic as it should have been. This year he made fresh serum, which he supplied to us for use, and that serum has been more favourable than any other we have used.

Major TOOGOOD: Following the remarks of the last speaker, perhaps I may be allowed to mention an epidemic, a small localised outbreak which occurred in the south-east of London. Clinically, all these cases were quite indistinguishable from cerebro-spinal fever of the meningococcus origin, but the organism which was isolated both from the throat and also from the cerebro-spinal fluid was a short bacillus of the zeroid type. As I say, clinically speaking, the outbreak exactly resembled that of cerebro-spinal fever, and yet the organism appeared to be entirely different.

Dr. HARRINGTON SAINSBURY: I think that during the prevalence of an epidemic of this type it is very important that we should investigate all cases of headache that persist. The second case Major ATKINSON referred to was under my care at the Military Hospital, Richmond, and I was puzzled over it. The patient did not seem particularly ill: there were no rigidities in neck or arms; no rash. I did lumbar puncture and obtained a fluid which looked rather doubtful, but which the bacteriologist's report shewed to be definitely meningococcic in nature. We thought the patient should make a good recovery, and this he did.

In cases of this kind which we clinically suspect, I do not think we should lay too much stress on the negative findings of the bacteriologist; I mean as to the presence of the meningococcus, for we are familiar in other forms of disease—definite tuberculosis, for instance—with negative results, although we know the disease to be present. Accordingly, if in doubt, we should proceed in our treatment upon the clinical findings. And here it is important to remember that simple tapping gives good results with a minimum of risk. I believe Major MICHAEL FOSTER, of Cambridge, treated most of his cases with tapping simply. However, though convinced that we have in tapping a very powerful means of combating the disease, I should always have recourse to serum if I could get it.

From another point of view, in regard to treatment, we should, in my opinion, proceed on clinical results rather than on bacteriological. I remember a case at the Royal Free Hospital, a sporadic case, in which the organism was found to be a pneumococcus. The patient, a boy, did extremely well on serum treatment, and the trouble appeared to be subsiding satisfactorily; then, for some reason, I did a tapping, and, to my surprise, found that the organism was still present. On the strength of this I gave a further injection of serum with rather bad results, suggestive of anaphylaxis; he had a definite set back. This made me decide, in this particular case, to proceed thenceforth on clinical lines only. The boy ultimately made a good recovery.

The question of the isolation of carriers of the meningococcus raises many difficulties, and I think we may have to be content to go upon reasonable rather than upon strictly scientific lines. It is not possible to isolate diphtheria carriers for the weeks and months of the persistence of the bacilli. It is not practical politics to do so. I think the same question arises with regard to cerebro-spinal fever, the germ of which may continue for months in the apparent presence of complete health.

Dr. F. HEWKLEY: May I ask if local treatment is of any efficacy, or, if the meningococcus cannot be isolated in the cerebro-spinal fluid, and a positive result obtained by examination of the pharynx, would local treatment by the use of the serum be at all expedient?

Major J. M. ATKINSON: There is no doubt that, with contacts, spray-

ing the throat, using a gargle of 1/1000 permanganate in 1·5 per cent. solution sodium sulph., will cause dispersion of the meningococci from the pharynx; also spraying the posterior naso-pharynx with a preparation of menthol, grs. viii.; iodine, grs. iv.; purolein, ad. ℥i.

Surgeon-General Sir DAVID BRUCE: Then you have no knowledge of the use of serum locally?

Dr. R. A. O'BRIEN (in response to the President's summons): I am afraid the only information I can supply bears on this very depressing question of the inefficiency of the serum we had in the early part of last year. From clinical accounts, I think there is no doubt that none of the sera available for treatment was of very great use. That was rather borne out by the examination of the serum in the laboratory. I do not know whether the strain of meningococcus occurring in England changed in any way. It looks as though they had, and yet when one compares them, one finds that most of the strains obtained to-day do correspond with the strains worked with years ago, *i.e.*, meningococci and para-meningococci. People who were making serum had the original strains of coccus, and they were immunising their horses with them; but it nevertheless remains a fact that all the serum available in the early part of 1915 had very little antibody reaction to strains isolated at that time. To-day it is all altered. Those in England who are making serum have obtained many strains from cases occurring on the Continent and in England, and are using them. Dr. FLEXNER very kindly sent me over some of his latest serum, obtained about the middle of the year, and it had exceptionally high content of antibodies. He had English strains sent over to America, and I believe that he found the earlier New York serum had a very low antibody content against such strains. Serum now obtainable in England has very high antibody content, and this is rather borne out by the fact that favourable clinical results have been reported from a number of sera now being used.

Surgeon-General Sir DAVID BRUCE: The Society owes a debt of gratitude to Major ATKINSON for his excellent description of the meningococcus. As far as my second-hand knowledge goes, his paper gives fully and accurately the facts as known up to the present day.

The question has arisen in the course of the discussion as to whether this coccus is the *causa vera* of cerebro-spinal meningitis. As far as one can see at present, there can be little or no doubt of this. It is true that cocci are a dangerous and elusive race, but this species is found so constantly in the cerebro-spinal fluid of cases of cerebro-spinal meningitis, that most workers agree that it must be the real begetter and originator of this disease. A fact which seems to me to carry a good deal of weight in this connection is, that when a particular strain or variety of the meningococcus is found in a particular epidemic, the same strain or variety is also found in the contacts. Some one has said "that no truth lasts longer than fifteen years," but I dare to prophesy that the life of this coccus will be longer.

Major ATKINSON told us that in regard to the relation of the meningococcus to this disease, KOCH'S three postulates have been fully satisfied. What about the third? At present the only way of setting up the disease in healthy animals by means of a pure culture is by injecting it into the cerebro-spinal canal, but many other organisms, if injected the same way, give rise to a similar inflammation. Until the disease is brought about by implanting the meningococcus on the mucous membrane of the pharynx, it can hardly be said that all three of KOCH'S demands have been fully answered in the affirmative.

In regard to vaccination against cerebro-spinal fever by the injection of the meningococcus, little has been done up to the present. Dr. PENFOLD, of the Lister Institute, carried out a series of inoculations at Salisbury, during the epidemic which occurred there a year ago, with what is reported to have been results suggestive of success. Lately, another opportunity occurred of testing the benefit of vaccination in a camp of Colonial troops, but Colonel GORDON informs me that although the epidemic ceased, there was no proof that this was due to the vaccine, as all the soldiers in camp were inoculated. There were no controls by which to test the results. On the whole, I think that the prospect of prophylactic inoculation against cerebro-spinal fever is favourable.

Lastly, as regards serum therapy. According to Colonel GORDON there are four strains of the meningococcus at present in England causing epidemics of cerebro-spinal fever. At one place an epidemic is caused by one strain, at another place by a different one. It then is necessary, in order to get good results, that a polyvalent serum got from horses,

immunised against all the strains, should be used. When it is known what strain is responsible for a particular epidemic, then, of course, a monovalent strain can be used. No statistics are as yet available, but I am informed that the treatment of cases by the polyvalent serum supplied by the Lister Institute has been highly successful.

Major J. M. ATKINSON: I thank you very much for your kind remarks on this paper. With reference to Fleet-Surgeon BASSETT SMITH's remarks, he asks, "How is it that people suffering from the disease themselves are not more infective." I think the reason is that the meningococcus in the naso-pharynx is so easily contaminated by contact with the saliva. It is difficult to understand the meningococcus coming from the pharynx without being contaminated by the saliva. In most cases of spitting, and even of kissing, contact with the saliva renders it in a very short time practically innocuous. This is the reason why they use West's swab in examining the nasal pharynx of contacts.

With regard to the four days, after finding two negative results, the contacts may be discharged to duty. A fairly trustworthy result should be available in four or five days.

I think one important point in the clinical history is the comparative slowness of the pulse with the high temperature; this is a very important diagnostic point. In each of these cases the pulse was 80° to 86° when the temperature was 101° F. and higher; another symptom is the intense headache met with in this disease. As Surgeon-General BRUCE says, one cannot form valuable deductions from a few cases; we have only had four cases, but I thought our experience might prove of interest.

MORPHIA INJECTOR'S SEPTICÆMIA (WHITMORE'S DISEASE).

BY

A. C. STEVENSON, M.B., D.P.H.,

Wellcome Bureau of Scientific Research.

The specimens shewn illustrate some points of the pathology of a disease which is fairly common in Rangoon, and in certain ways resembles glanders, but which differs from that disease in there being no skin lesions and in the character of the organism causing it. The disease, first described by Major WHITMORE, was first noticed in a man who had the morphia habit. As it appears to be commoner in such people, it received the above name, but it is not confined to such cases.

Attention was drawn to the disease by the first post-mortem appearances seen—the nodules in the lung; but nodules may also be found in the liver, kidneys, and spleen, while the lungs may be free. When near the surface of the organ, these nodules shew as yellowish areas, surrounded by one of redness, and feel distinctly firm to the touch. On section, caseation is suggested by the appearance, but this practically never goes on to softening, except in a very small way.

Microscopically, the caseating area is seen to be made up of largely distended alveoli, filled with polymorphonuclear and mononuclear leucocytes and endothelial cells. In some areas these are seen to be necrotic. The red area is one of engorgement of the blood vessels and hæmorrhage into the alveoli.

Amongst, and in the leucocytes in the alveoli, small beaded bacilli are seen. They do not retain Gram's stain, nor are they acid fast. Their length and the number of beads in them vary considerably. When cultivated on ordinary media they appear as short rods, with generally two dark staining dots in them; on salt agar they grow into long filaments. They are motile in the early stages of cultures, but this soon disappears.

Inoculation into guinea-pigs invariably leads to a fatal result with the formation of nodules. If only a small dose is used, $\frac{1}{2}$ to 1 minim of an 18 hours' broth culture, intraperitoneally, enlargement and inflammation of the testicle is got, as in Strauss' sign in glanders, in about 36 hours. With large doses death ensues too quickly. Guinea-pigs are also capable of infection by feeding with cultures.

A full account of the disease and its pathology can be found in an article by Major WHITMORE in the *Journal of Hygiene* of April, 1913, to which I am indebted for what knowledge I have.

The specimens and the parent culture of these shewn was a present to the Bureau from Dr. L. G. FINK, of the Rangoon General Hospital.